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RADIUM

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VOL. XVIII MARCH, 1922 No. 6

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THE PROPERTY OF THE ACADEMY OF MEDICINE TORONTO 13 QUEEN'S PARK

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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Edited by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. XVIII **MARCH, 1922** **No. 6**

A REPORT OF THE WORK OF THE RADIUM DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA HOSPITAL, BETWEEN APRIL, 1920, AND APRIL, 1921*

By LAURENCE R. TAUSSIG, M. D., San Francisco, Director of the Radium Laboratory of the University of California.

The purpose of this report is to place before the members of the medical profession a brief account of the policies and activities of the radium department during the year following the installation of a radium emanation plant at the University of California Hospital. In the early part of 1920 an order was placed by the University for an amount of radium sufficient to bring the total supply up to about 650 milligrams. At the same time a plant for the purification and tubing of the emanation was ordered. This plant was put in operation with a little over 600 milligrams of radium element in solution early in April and has been operating steadily ever since except for a few shutdowns to remedy minor breakages.

When the emanation plant was installed it was thought by a number of medical men that the supply of emanation would be practically unlimited and that it would make radioactive applicators available to anyone desiring them. This, of course, is not true. The amount of emanation on hand at any one time cannot exceed in activity the amount of radium in solution, and for a number of reasons, this maximum is never reached. It would be unwise to diminish the total amount available by the outright sale of any of the tubes. The radium committee decided

*Reprinted by permission from the California State Journal of Medicine, XX, 50-51, February, 1922.

that it should be applied only under the supervision of a member of the radium staff, in order, insofar as possible to insure the best results. Clinic and ward patients, treated at hospitals affiliated with the university, are charged according to their circumstances. This charge is set by the social service department after appropriate investigation. Many of these patients receive treatment gratis. Private patients, either in the university hospitals, or in other hospitals, are treated only in consultation with a member of the radium staff and are charged a definite fee according to the amount of emanation used. Private cases which are sent from medical men out of town are treated according to the indications as determined by any further examination deemed advisable and are referred back to the physicians sending them with suggestions for the after treatment as well as an account of the findings and methods of treatment employed. It is the policy of the department to answer inquiries from members of the profession as to the suitability of specific cases for radium therapy as definitely as possible. It is hoped that physicians, whether they possess radium of their own or not, will not hesitate to inquire about points in technique. Furthermore, visitors are always welcome to inspect any part of the work which interests them.

It is not the purpose of this report to go into the technique of the application of radium. In the future, as data accumulates and definite conclusions can be reached in the light of carefully kept records, papers will be published, detailing technique and results in specific groups of cases. At present the number of cases treated during the year will be given, with a general statement of the results obtained in each group. Insufficient time has elapsed to attempt to classify the end results because the majority of these cases are of malignancy.

Basal Celled Epithelioma—91 cases. The results in this type of malignancy continue to be eminently satisfactory. Radium therapy is especially satisfactory in the more difficult cases, particularly in those located at the canthi or on the lids of the eyes. The very extensive and long standing cases of this variety of epithelioma can also usually be improved if not cured.

Squamous Celled Epithelioma (of the glabrous skin)—20 cases. The primary lesion can usually be healed at least temporarily if not too extensive or if it has not been previously treated. Metastases in these cases are frequent and the end result in a given case is therefore in doubt for some time after finishing radium treatment.

Carcinoma of the Lip—15 cases. These cases have only recently been submitted to radium therapy. So far the results have been very encouraging. Radium should be combined with surgery and x-ray in many of them in preventing and in treating cervical metastases.

Carcinoma of the Mouth (exclusive of carcinoma of the tongue)—25 cases. When the lesion is not too extensive, a marked improvement can be obtained in some of these cases. The technique of treating mouth cases is changing and with the availability of the emanation the results have been improved.

Carcinoma of the Tongue—17 cases. Most of these were advanced cases. In the earlier cases the healing of the tongue lesion is the rule and even in late cases judicious therapy often effected considerable palliation. The main problem is the handling of metastases.

Carcinoma of the Oesophagus—5 cases. Improvement can be obtained in nearly all of these cases by the combination of the x-ray and

radium therapy. This improvement consists in temporary relief of dysphagia, pain and cough with gain in weight and strength.

Carcinoma of the Cervix—38 cases. Radium is of benefit in all but very extensive cases and recurrences. Post-operative radium therapy has been abandoned.

Lymphosarcoma—7 cases. Radium in these cases is superior to x-ray only when the tonsils are involved or the growth is of limited extent. Temporary relief is usual, though recurrences generally occur.

Sarcoma—16 cases. Rapidly growing sarcomata react quickly to radium therapy, but recurrence follows a brief period of quiescence in most of them.

Keloid—4 cases. All but long standing cases can be greatly benefited.

Keratosis of the Lip—8 cases. These are potential carcinomata and should be treated as very superficial malignancy. Radium has proven very satisfactory.

Lupus Erythematosus—10 cases. In the chronic discoid type of this disease radium is often of considerable benefit.

Lupus Vulgaris—5 cases. No other form of therapy surpasses radium in treating even extensive and long standing cases of this disease.

Vascular Nevus—19 cases. In the raised type a good cosmetic result is the rule, but in the flat port wine stain type a slight paling is all that can be hoped for.

Verrucae—5 cases. In certain regions radium is the treatment of choice. This applies particularly to those near the finger nail and to verruca plantaris between the toes.

Grave's Disease—11 cases. The result is earlier and more marked than in any other form of therapy. Whether the effect is permanent or not cannot yet be stated. Radium is not suitable in treating toxic adenomas.

Incipient Cataracts—60 cases. A large percentage of these have been given improved vision. Radium is useless in mature cataracts.

Miscellaneous—56 cases. This includes the cases which do not fall into any of the above groups, and in which the treatment with radium has been more or less experimental.

Thus 420 cases of various types have been treated during the year and though many of them are of the most hopeless in the realm of medicine, the results have been encouraging. New fields are being opened to radiotherapy by changing methods and improvements in technique are leading to better results. The use of the emanation instead of radium element has proven eminently satisfactory. The advantages far outweight the few disadvantages and make the use of emanation preferable.

REVIEWS AND ABSTRACTS

Francis Carter Wood, M. D. (New York.) Biological Determination of Radiation Dosage. The Journal of Radiology, iii, 37-39, Febru-

ary, 1922. Read at the Annual Meeting of the Radiological Society of North America, Chicago, December 7, 1921.

"The attempt to treat deep-seated neoplasm with highly filtered rays has led to a realization of the fact that in order to obtain any permanent results, doses much larger than have previously been used must be given. Owing to the necessary limitation of the number of portals through which the exposures can be made, the dose which the skin receives must be terminated just at the point at which a slight erythema appears, or, according to some workers, in such excess of erythema as is possible without producing irreparable damage to the skin. If this latter dose is in any way exceeded, very severe and even permanent injury to the skin may result. These statements are true, whatever type of machine is employed and are also true of any voltage which may be employed."

"There is no evidence to show that the burns produced without a filter or with low degrees of filtration are any more severe than those produced by the use of thick copper filters and the highest voltages now obtainable."

"The only point is that in the first instance it is easily possible to give four or five erythema doses in a few minutes, while with the higher filters and voltages, hours are required instead of minutes to exceed the proper limits of skin exposure. This, however, is true that with long skin distance and high filtration the high percentage depth dose which is possible under these conditions, may result in deeper sloughs. In any case it is evident that the possible skin dose is the limit to the exposure for a given area."

"The determination of such dose becomes, therefore, a matter of primary importance before deep therapy can be properly administered as insufficient raying stimulates tumors instead of retarding their growth."

"With heavy filters of any of the metals employed the methods previously used to determine dosage are extremely unreliable. The stimulation of the characteristic radiation of silver at about twenty-five K. V. renders photographic methods misleading. A similar error attends the use of pastilles containing barium and platinum, in addition to the fact that such pastilles are insensitive to short wave lengths."

"Simple and accurate ionization chambers are not at present available. The use of types such as may be found in any physical laboratory implies the employment of electoscopes or highly sensitive galvanometers. In addition, their readings are by no means necessarily indicative of the biological dosage. With the advent of more powerful x-ray apparatus yielding voltages of two hundred thousand and over and a vastly larger output of x-rays through thick filters, the development of a convenient method of determining not only the skin dose, but also the amount reaching the tissues at a considerable depth, is imperative."

"Unless the depth dose is known, it is perfectly possible by using four or five portals to adminster sufficiently large amounts of x-rays so as to cause serious injury to internal organs or even to induce sloughing of the walls of the hollow viscera with fatal results. Fortunately, some types of cancer, though not all, are more susceptible to rays than normal tissues, a point about which develops all possibility of effective radiation treatment. But often the border line is a very narrow one; hence dosage must be accurate."

"At present the only way for the x-ray therapeutist to estimate the proper dose is to determine the skin erythema with given sphere gap voltage, milliamperage, skin target distance and filtration. This is time

consuming, and if the limit is accidentally exceeded annoying results may eventuate. After this, recourse must be had to tables of dosage such as are published in current journals or in pamphlet form by Voltz and others. Measurement of the patient an destimation of the depth from the surface and thickness of the tumor give the other necessary data. The limits of error are evidently considerable and how much simpler the matter would be if a direct reading of all these factors could be obtained by an ionization chamber of such dimensions that it could, if necessary, be placed in contact with the tumor, if cervical, rectal, or prostatic, or under the patient if abdominal or thoracic, and direct readings in biological, not physical, units obtained."

"With the scientific knowledge already available in this country such an apparatus could be designed and calibrated with a standard biological material and if a sufficient demand existed a number of firms in this country have the technical force available for their construction. I should like to see such an apparatus regarded as the essential part of the equipment of every one attempting deep therapy. Without such equipment comparable results are not obtainable and the successful therapy of those types of deep cancer amendable to x-ray delayed for another generation."

"What are the scientific data necessary for the production of such a standard apparatus?"

"It has been often stated that the radiation effect on the cell is in direct proportions to the amount of energy absorbed by the cell. The amount of this energy for different wave lengths cannot as yet be accurately determined by physical means, but using an ionizing chamber of aluminum, experiments conducted in the Crocker Laboratory have shown that equal ionization doses of unfiltered and of variously filtered rays do not have equivalent lethal effects on animal tumor cells. This has been confirmed by Kronig and Friedrich, who, however, demonstrated that with a chamber made wholly of horn and graphite, equivalent ionization doses had the same effect on tadpoles, on germinating seeds, the ovary and on the human skin, but they did not try animal tumors. It cannot as yet be considered absolutely settled that equal ionization doses are equally effective, no matter what the wave length of the x-ray. While it is probable that Kronig and Friedrich are correct, there are many who still believe otherwise."

"Our nearest approximation to a biological standard now in use is the skin erythema dose. This, however, varies in individuals and over different portions of the body, as is well known, but as it furnishes the limit of all deep therapy it is still our only practical unit. Once obtained it is easily reproducible with the same x-ray apparatus under exactly the same conditions of working. It cannot, however, be necessarily transferred to any other make of apparatus, by any process of arithmetic. The yield of the tube depends upon many factors; the wave form which in turn depends upon the construction and adjustment of the rectifying switch, the transformer characteristics, and many other variables. Each machine must, therefore, be checked upon a human being, as has been said, which is time consuming, and if the limit is exceeded may produce permanent injury. If, however, some constant biological material was available which required a given x-ray or radium dosage for its destruction, it would be easy to calibrate an x-ray machine or an ionization apparatus which would in turn exact control over the workings of the machine."

"Such a test object is available in one type of the transplantable tumors of animals. Those suitable for this purpose are transplantable in a high percentage in all breeds of white mice, and practically do not regress, except in rare instances. The animals are cheap and easily kept. They can be inoculated with the tumor and when this has reached a convenient side, it may be exposed to a dose some multiple of the assumed erythema. The strain upon which the largest number of observation have been made is Crocker Fund 180 and with it this factor is five. *After the exposure, the tumor is excised and bits are grafted on a series of animals. If the dose is correct no tumors will appear. If too low, some will come up after a few weeks, or months, greatly slowed in their growth rate. Another tumor can again be exposed for a slightly longer time, and thus by a few trials the mouse tumor dose determined."

"Such a test is more time consuming, however, than the determination of the erythema dose and obviously cannot be generally used. It would be far better if the x-ray apparatus could be biologically calibrated by the maker before it left the factory."

"This lethal tumor dose has been determined on No. 180 for four successive years, using the same machine, which has not been altered in its adjustment, and checked with the same ionization chamber and has not varied. The deflections of the galvanometer have been within a couple of millimeters of the same point each time the machine has been run. It is made of aluminum after the design of Professor Wm. Duane. Recently a new set of machines of much higher power were installed under my supervision in another institution. Using the same voltage, distance and filters, and adjusting the current to give the same ionization deflection, the tumor was killed in the same time, as with the older apparatus, and the erythema dose on human skin was also found to be the same. With these factors available, the erythema dose for varying distances, voltages and filters was quickly obtained and in a few weeks the plant was treating effectively a large group of patients, with heavy dosage, yet without skin burns. For example—the lethal tumor dose at 166 K. V. 5 M. A. 40 cm. distance, 0.5 mm zinc and 1 mm. aluminum was found to be 180 minutes. The erythema was posted as a safe limit for the staff as not to exceed one-sixth of this, or thirty minutes to start with. Careful checks on patients have shown that under these conditions and true erythema is between thirty-five and forty minutes, depending upon the region treated."

"The erythema dose which we use is a faint reddening produced on the skin of the chest or abdomen after seven to ten days, followed by slight desquamation and ultimate browning. It is apparently the same as that of Seitz and Wintz, but not more than half of that used by Warnekros, who defines an erythema dose as such an amount as will not cause irreparable damage to the skin. The Warnekros dose, of course, causes skin atrophy and telangiectasis and should not be used in exposed portions of the body, and is so near the limit of permanent damage that it cannot be repeated on a sensitive skin."

"The mouse tumor dose, however, is a fixed quantity and not variable like the erythema. It is determined by one fact only, the death of all the tumor cells. If any survive, a tumor will grow from the transplant."

*The details of these experiments have been published in the Jour. A. M. A., 1920, LX. They have been repeated in Germany Kysser and others, who are, apparently, unaware of our work. The lethal dose with radium for this tumor was also published in the Annals of Surgery, 1915.

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"Can the fact that a highly malignant mouse tumor requires five erythema doses to kill all the cells at one treatment, be used as a guide to the therapy of tumors in man? I believe that it can, and should. The resistance of this tumor is comparable to that of the more malignant types seen in man, such as the tumors of the intestinal tract, the squamous celled epitheliomata, but it is less than that of the melanomata and many of the bone and periosteal sarcomata in man, which often resist extraordinarily large doses. A slow growing fibrosarcoma of the white rat (Crocker Fund 37) for example, requires some eight erythema doses to kill it. Other animal tumors, however, may be killed with two or two and one-half doses, and correspond to the more susceptible growths seen in man."

"It is very dangerous to assume that the proper carcinoma dose for human therapy is that which results in the destruction of a subcutaneous metastatic nobule from a carcinoma of the breast, as Kronig and Friedrich are careful to point out. They say that such disappearance may be only temporary after their "carcinoma dose" and recurrence take place later. This statement seems to have been overlooked by many writers who have assumed that the "carcinoma dose" necessarily means a curative dose. The conditions are entirely different from the primary tumor. The metastatic nodule, as shown by animal experiments, is certainly at least twice as susceptible and this susceptibility is probably due to the surroundings, imperfect vascularity, etc., of the embolic particle. When freshly deposited it will often disappear after the erythema dose, but if it does not every x-ray worker knows that at least a burning dose, say one and five-tenths skin erythema doses, is necessary, and when invasion of nearby bone or cartilage has taken place a still higher dose is necessary. Even a basal-cell carcinoma, the most benign type we know, is more difficult to handle after it invades bone or cartilage. It is often loosely assumed that the cells have become "immune"—an utterly illogical assumption."

"The fact that mouse tumors which have been exposed to nearly lethal doses in the animal's body, and then allowed to remain for ten days before inoculation, show a much lower percentage of takes than when they are immediately transplanted, has been cited as showing, but does not prove, that the tumor cells have been killed by any tissue, or immunity, reaction. It merely shows that when the transplantation is done immediately the cells are still in a healthy condition, and, therefore, the few which are going to survive are able to get started before the radiation changes begin, for it only takes about four days for a graft to organize its blood supply. If, on the other hand, the tumor is transplanted after eight or ten days, when the cells are all seriously injured by the development of the full x-ray or radium effect, the graft is in no condition to withstand the trauma and partial necrosis which such grafts always undergo when transplanted into a fresh soil before the capillary supply is organized."

"Cancer cells do not become immune to repeated radiations, for if a mouse tumor is rayed with a sublethal dose and inoculated and again rayed and inoculated, and this process repeated a number of times, it still may be killed at the end of the series with exactly the same dose as at the beginning. The fact is rather that the cells of the resistant tumor are just the same as before, but that it is now impossible to attack the tumor through its blood vessels, which is all we do in many instances. The cells lie diffused through an avascular connective tissue,

and while some may be killed, others remain to grow again at a much later period."

"This is the condition so often noted when a tumor has previously been treated with radiation or caustics, a notoriously unfavorable condition. There is no evidence that the tumor cells have changed or become more resistant."

"The carcinoma and sarcoma doses of Seitz and Wintz, or Kronig and Friedrich, are, therefore, not generally applicable to all tumors, only the lymphosarcomata, and the basal cell carcinomata are permanently curable with an approximate erythema dose, and even these tumors occasionally show full resistance. Many, though not all of the carcinomata of the cervix, however, seem to be much more susceptible to radiation than tumors of similar morphology in other parts of the body. While an occasional lymphosarcoma will be permanently cured, it is too often multiple and inaccessible to offer anything but an accidental cure. The skin and cervix tumors are at present the great field for radiation, though if easily operable, both should be removed, to be followed by prophylactic raying. How difficult judgment is in these matters, and how imperfect as yet our knowledge of biological dosage and preferable technique is illustrated in the somewhat active discussion now going on in Germany concerning the value of what has been generally assumed was one of the best established fields for the x-ray, that is, post-operative raying after carcinoma of the breast."

"CONCLUSIONS—I. It is extremely difficult to properly calibrate an x-ray machine for deep therapy as the difference between a stimulating and inhibiting dose for tumor cells is not very great, while the difference between the dose necessary to inhibit or kill may cause serious injury or even death of the patient is also unfortunately very small."

"II. Exact surface and depth dosage is, therefore, a necessary preliminary to deep therapy. This is rendered difficult at present by the lack of suitable instruments calibrated in biological dosage such as a standard skin erythema."

"III. The best way to calibrate such an instrument when constructed is by the use of a mouse tumor of constant and tested biological qualities. Such a tumor is the Crocker Fund No. 180. In five years of study, it has shown no variation in its x-ray lethal dose and this tumor takes in practically one hundred per cent, grows rapidly and regresses in only a fraction of a percent in mice of any available market stock."

"IV. The lethal dose for this tumor for x-ray of any voltage and any filtration is approximately six erythema doses as measured by a faint redness after ten days on the most sensitive skin areas. About five doses for heavily pigmented skin of the back and about two and one-half to three severe erythemas of the Warnekros standard."

"V. In comparison to human tumors, it shows about the same resistance to x-ray as the highly malignant neoplasms of the intestinal tract which as yet evade successful radiotherapy."

"VI. The lethal dose for radium for this tumor being also known, it furnishes the means for a biological comparison between the action of x-ray and radium and permits the estimation of equivalent dosage."

* * * *

Francis H. Williams, M. D. (Boston). Treatment of Hypertrophied Tonsils and Adenoids by Radium, a Preliminary Statement. Boston Medical and Surgical Journal, clxxxiv, 256-257, March 10, 1921.

"The excellent paper recently published by Drs. Murphy, Witherbee, Craig and Hussey, entitled, "Induced Atrophy of Hypertrophied Tonsils by Roentgen Ray," is interesting and instructive, but treating the tonsils from "under the angle of the jaw" and the adenoids "through the back of the neck" is open to the criticism of exposing to the rays other parts than those it is desired to reach. The rays from radium also act on the lymphoid tissues, of which the tonsils and adenoids are made up to a large extent, and can be applied directly to the tonsils and adenoids, the neighboring parts being protected by lead, that is to say, the radium container is covered with lead except on the side through which it is desired that the rays should issue. When as above, roentgen rays were used, the maximum amount reached other tissues than the tonsils and adenoids; when radium is employed, the maximum radiation reaches the tonsils and adenoids, and the minimum other parts. Another advantage of radium is that the output is constant, and the dosage can be exact."

"I have used 50 milligrams of bromide of radium* in a flat container, with the rays filtered by 0.83 millimetre of aluminum, held directly against or near the tonsil. The radium should be withdrawn every few minutes, or as often as is comfortable for the patient, until the total exposure of fifteen minutes, more or less as required, has been reached. Improvement follows promptly, but the ultimate results may be expected only after some weeks. Guided by more than seventeen years' experience in the use of radium, it seems to me better not to attempt complete healing by one treatment, for the present at least, but rather to give two or perhaps three treatments at intervals, as patients and conditions differ."

"It may prove more convenient to use a container by means of which both tonsils may be treated at the same time. I have devised one to be held midway between the tonsils, which consists, in general, of a disk of lead (not more than 2 cm. in diameter and about 1 cm. thick, more so in the middle) with a hole bored through its center, somewhat flared at each end, for the exit of the rays, and another bored from the outer edge radially to a little beyond the center. The tube containing the radium may be slipped into this and the opening afterwards closed by screwing a metal handle part way into it. The uvula, the back of the throat and the parts behind it are thus protected by about 1 cm. of lead. When treating one tonsil only, the opening towards the other may be closed with a plug of lead. Appropriate filters should be used."

"Before applying the radium, the throat should be moistened with a suitable solution of cocaine to prevent gagging from the insertion of the container. All instruments should be covered with two thicknesses of rubber, and for this purpose two rubber finger cots are stretched over them and far down on the handle, where they may be secured by a strip of plaster. Of course, fresh cots should be used for each patient."

"In using this method I have thus far treated the tonsil only, as the results there may be more easily observed than in adenoids. These may be reached through the nose by a small instrument, carrying radium, from the end of which the rays issue upwards."

"Adenoids can also be reached by directing the roentgen rays upon them through the nose instead of through the back of the neck as de-

*Equivalent to 53.6 mgm. of radium element.—Ed.

scribed in the article referred to above. This treatment might be carried out, for example, by distending the nostrils with a special bivalve speculum, one blade inserted horizontally in each nostril, and by protecting the skin inside the speculum with oxide of zinc plaster and that outside by sheet lead. In this case the length of exposure would be shorter, for children only about one minute, then when the rays are obliged to traverse a large amount of dense tissue, and the risk of burns would be far less."

"The disadvantages of operation are obvious. The roentgen rays should be employed only by physicians who have had experience in their use."

"It is, of course, too early to make a definite statement concerning the comparative value of operation, roentgen rays, and radium. For adenoids the roentgen rays and radium—treatment by both of which is painless — may each be of service in a special group of patients. For the tonsils, radium, if properly used, I consider the safest and that it will probably prove to be the best treatment for many patients."

"While not coming within the title of this paper, it is noteworthy that after treatment by radium, I have observed striking improvement in acute and sub-acute tonsillitis."

* * * *

Frank C. Benson, Jr., M.D. and Joseph V. F. Clay, M.D., F.A.C.S. (Philadelphia). A Case of Parinaud's Conjunctivitis Treated With Radium. Journ. Ophth. Otol. and Laryngol., May, 1921.

"The case we wish to report is one offering much of interest from a diagnostic standpoint, and also most interesting evidence of the beneficial therapeutic effects of radium. The local medicinal management of the condition was one series of discouraging events and it remained for radium to perform one of its many triumphs in a most distressing and stubborn ocular lesion."

"The patient, a female, aged 72 years, had had an attack of follicular conjunctivitis in August, 1915. In this attack she was treated by the late Dr. G. W. H. Conrad, whose record of the case we have had the privilege of reviewing. From Dr. Conrad's description of the condition we must concur in the diagnosis. This attack followed surf bathing and yielded promptly to treatment. In May, 1917, she had a mild attack similar to the first. In September, 1918, she consulted us because of photophobia, lachrymation, and discharge from both eyes. At this time the palpebral conjunctiva, especially of the lower lid, presented a marked smooth, velvety, thickening. This yielded to boric acid powder massage. Ten months later, August, 1919, there was a return of symptoms in a sub-acute form, in the right eye only, the palpebral conjunctiva presenting a marked thickening, with small polypoid elevations on the bulbar portion. This attack resisted all local treatment, and in October the cornea presented a pannus. The conjunctiva about the semilunar fold became hypertrophied and thrown into folds. In January, 1920, there occurred an apparent acute exacerbation, there being a marked increase in the lachrymation, photophobia and discharge, of a mucoid character, and in addition severe aching pain through the

right eye and right side of the head. Associated with these local symptoms were marked prostration, fever and enlargement of the pre-auricular and posterior cervical lymphatics. The conjunctiva was now engorged and thickened to such an extent that the patient was unable to raise the upper lid. Eversion of the upper lid was exceedingly difficult owing to the tremendous thickening of the conjunctiva, which presented cobbled-like elevations, varying in size, and of a yellowish red color. The bulbar conjunctiva was equally involved, and at the semilunar fold a polypus-like mass presented. The cornea, while clear, appeared buried in a velvet-like cushion of conjunctiva. The iris was normal, the pupil reacting readily. A spicule lenticular opacity was noted, otherwise the ophthalmoscopic findings were negative."

"Local applications seemed to have no influence upon the condition, or in relieving the distressing subjective symptoms. During this time the left eye remained absolutely free."

"A section of the hypertrophied conjunctiva was removed from the lower lid near the globe and submitted to Dr. S. W. Sappington for microscopical study. Four sections were made, and the report states that each section showed identical conditions, purely lymphoid tissue. The tissue was of the same form as ordinary lymph follicles, with peripheral concentration of small lymphocytes and central paler germ centers, but the greater part of the sections showed a diffuse monotonous spread of lymphocytes of the germ-center type, without any special arrangement. Capillaries with very thin walls were seen here and there among the cells and immediately beneath the surface; the capillaries were so numerous as to constitute a small network. No giant cells were seen. Necrosis and caseation were absent and there was no evidence of tuberculosis or anything to suggest tumor growth."

"The differential diagnosis of the various conditions suggested by clinical manifestations and the histological study of this case is interesting and not without difficulties. Tuberculosis and trachoma are the diseases most closely suggested and the ones usually confused with Parinaud's disease. There is perhaps much to be desired in the way of evidence favoring the diagnosis of the latter condition in this case, and yet it seems to lend itself more strongly to Parinaud's than to tuberculosis or trachoma."

"According to Morax the infective organism of Parinaud's disease has not been discovered, and clinical features alone are not always sufficient to make a differential diagnosis. Histological examination must determine whether the conjunctival condition is one of the lymphatic glands. The diagnosis of Parinaud's disease should be reserved for those cases in which the absence of giant cells and negative results of inoculation and culture justify the elimination of tuberculosis or sporotrichosis. If the histological examination shows giant cells, it is either tuberculosis or sporotrichosis. Inoculation will differentiate tuberculosis. Culture on usual media will show the typical cultural characteristics of the S. Beurmanni. If no giant cells are found the condition must be differentiated from syphilis."

"Trachoma usually attacks both eyes, while tuberculosis and Parinaud's disease are more frequently observed in one eye. Bulbar follicles are uncommon in trachoma; in Parinaud's disease they are common. Trachoma is observed at any age as is also Parinaud's disease, while tuberculosis favors youth. Trachoma results in scarring; Parinaud's disease does not produce scars."

"As regards subjective symptoms, our case was unlike any of these diseases. In tuberculosis, unless it be ulcerating, there is little or no distress. Likewise in trachoma, there is little distress aside from the visual disturbance. Parinaud's disease usually presents few or no subjective symptoms. Our case was acutely disturbed by the subjective symptoms, and at no time did we observe irritation of the uveal tract until after the second application of the radium."

"As regards the course of the condition, Parinaud's disease, it is claimed, tends to a spontaneous recovery within a few months. Tuberculosis is a very chronic disease lasting over a period of years. Trachoma is also chronic in its course, with at times intermissions and exacerbations until complete cicatrization occurs."

"After a careful study of the clinical features, together with a consideration of the histological findings, as reported by Dr. Sappington, we concluded to apply radium, for the same action as procured in non-malignant papilloma of the urinary bladder."

"Fifty mgm. of radium element, screened with 0.05 mm. of silver, were used on alternating days for exposures of one hour each (two exposures of 100 mg. hrs.) until the inflammatory reaction appeared. While much larger amounts of radium and longer exposures are made use of in the treatment of new growth-formation, greater screenage is always used and it must be remembered that with even relatively small quantities, inadequately screened, serious destruction of tissue may follow even short exposures. Such inadequate screenage allows not only the escape of the alpha and beta rays, but also of the secondary (Sagnac) rays; all of which may be prevented by the use of sufficient filtering media. From the foregoing it may be seen that it was our desire to set up a change in the afferent blood-supply of this condition, at the same time stopping short of a reaction which would result in destruction of tissue sufficient to cause scar-formation."

"After the second application of radium the eye became markedly injected and chemotic, the nodules appeared flattened, the cornea hazy, the iris discolored, the pupil contracted and inactive. Atropin 1 per cent. was instilled for two days with the application of cold compresses. At the end of two weeks all subjective symptoms had entirely disappeared. At the end of four weeks the pannus had cleared and the hypertrophied follicles were gradually disappearing from the bulbar conjunctiva, receding from the limbus in a circular manner as if they were melting away."

"The patient has reported to us at intervals of a month since the application of the radium, and each visit a progressive lessening of the thickened tissue has been noted. At this writing, January, 1921, the patient is perfectly comfortable; there has never been the slightest tendency to recurrence of symptoms. The lid action is now normal. The palpebral conjunctiva is still thickened but smooth and without scar. There is a small area of thickened conjunctiva upon the bulbar area to the lower temporal side. The cornea is perfectly clear and—of interest in passing—the lenticular spicule is not discoverable at this time. If the change in the lenticular spicule was the result of the action of the radium used, it must have been due to the gamma ray selective alterative action."

"Since the application of the radium a simple boric acid lotion has been used morning and evening."

Dr. Benson reports the patient still well January 26, 1922.

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